

### **REMARKS/ARGUMENTS**

In this Amendment, claims 58, 60-64, 68-70, 73, 75-77, 84, 86, 89, 93, 95 and 103 are currently amended; claims 65-67, 81-83, 87, 88, 90-92, 98-102 and 104-106 were previously presented; and claims 1-56, 57, 59, 71, 72, 74, 78-80, 85, 94, 96 and 97 are canceled without prejudice or disclaimer. Claims 107-121 are newly presented. It is submitted that no new matter has been added by virtue of the amended and new claims, which are supported by the original and prior claims and by the disclosure of the application as originally filed. Accordingly, the currently pending claims are now claims 58, 60-70, 73, 75-77, 81-84, 86-93, 95 and 98-121.

#### **Support for the amended and new claims**

New claim 107 replaces prior claim 57 and is supported by the instant specification, e.g., pages 9 and 10, as well as by prior claim 57. Support for new claims 108-110 and 114 is found in the disclosure of the instant specification on page 9, lines 22-37 to page 10, lines 1-24. Support for new claims 111-113 and 115-121 is found in the instant specification and in the prior and pending claims.

It is submitted that in the Remarks below, the 05/10/05 Office Action has been considered as if it pertains to newly presented claims 107-121. Thus, this Amendment is intended to be responsive to the 05/10/05 Office Action as if it applies to the new claims.

#### **The claims satisfy the requirements of 35 U.S.C. §112, first paragraph**

Claims 57, 58, 60-84 and 86-106 were rejected under 35 U.S.C. §112, second paragraph, as allegedly failing to comply with the written description requirement. The Examiner mentions that claims 60 and 88 define specific reactions and further states that "the specification/written description does not describe how a carrier undergoes a chemical reaction in the invention."

Applicants respectfully disagree with the Examiner and point out that the instant specification/written description does describe how a carrier undergoes a chemical reaction according to the present invention. It is submitted that Applicants' original specification provides an explanation of chemical operations, which generally involve one or more chemical reactions, such as those described on page 12, lines 5-6 of the instant specification.

Additionally, on page 9, lines 11-21 of the specification, it is disclosed that

... the term "chemical operation" refers to a measure resulting in formation or cleavage of covalent bonds. Said formation or cleavage may comprise of by indirect means yield a pH change of the composition, thus involving a proton transfer which in some cases may be regarded as formation or cleavage of a covalent bond. However, such a pH change is in this context the result of a chemical operation which does not merely comprise a proton transfer but which also comprises formation or cleavage of other types of covalent bonds.

As taught by the instant disclosure, the conditions for performing a chemical reaction in accordance with the present methods are known by those having skill in the art and are as described in the standard reference literature. (*See*, page 13, lines 16-21 of the instant specification). Preferred embodiments of the present invention in which suitable chemical reactions such as esterifying and polymerizing are employed are described in the instant specification on page 13, lines 1-15; on page 14, lines 16-23; on page 16, lines 17-37; and on page 17, lines 1-20.

As further described by Applicants, the performance of a chemical operation in Applicants' methods, i.e., by performing one or more of the disclosed chemical reactions, results in the formation of a liquid or solid non-crystalline carrier matrix in which the biologically active agent is present at an increased degree of saturation. The instant specification also discloses that the degree of dissociation, aggregation and/or degree of protonation of the biologically active agent can be different from the degree of dissociation, aggregation and/or degree of protonation of the biologically active agent in the carrier starting substance(s)." (*See*, pages 10, lines 32-37 to page 11, lines 1-14 of the instant specification).

Moreover, on page 13, lines 7-25, the instant specification particularly describes how a desired non-crystalline carrier matrix may be formed when an esterifying chemical reaction is performed on multifunctional starting carrier substances. The specification further teaches that polymerization of starting carrier substances is another chemical reaction suitable for use in the method of the present invention. Additional description of chemical reactions that involve carrier substances according to the present invention is found on page 14, lines 16-31.

In view of the foregoing, Applicants respectfully submit that the instant specification/written description clearly discloses and describes various ways in which a chemical reaction involving carrier and/or a biologically active agent is performed in accordance with the presently claimed invention. Withdrawal of this rejection is thus respectfully requested.

**The claims satisfy the requirements of 35 U.S.C. §112, second paragraph**

Claims 57, 58, 60-84 and 86-106 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Examiner remarks that when the composition in step (a) of claim 57 "is recited as one carrier, it is not clear how that can be a composition." Applicants' respectfully submit that the cancellation without prejudice of claim 57, the presentation of new claim 107 and the currently amended claims dependent thereon moot this rejection. Accordingly, withdrawal of the 35 U.S.C. §112, second paragraph rejection is respectfully requested.

**Objections to the Claims**

Claims 95-97 have been objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form for allegedly failing to further limit the subject matter of a previous claim. It is respectfully submitted that the present amendment to claim 95 and the cancellation without prejudice or disclaimer of claims 96 and 97 moot this objection. Withdrawal of the objection is thus respectfully requested.

**The claims satisfy the requirements of 35 U.S.C. §102**

Claims 57, 58, 61, 62, 64-75, 78-84, 86, 87, 89-97, 100-102 and 105 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by U.S. Patent No. 5,906,830 to Farinas *et al.* (hereinafter "Farinas").

The Examiner remarks that the method of Farinas "comprises mixing polymeric material and a drug formulation, removing the [*sic*] most of the solvent, evaluating the depressed melting temperature of the drug-polymer mixture, heating the mixture to a predetermined temperature and cooling the heated mixture to form the supersaturated reservoir (claim 1)." The Examiner further remarks that Farinas "does not specifically state a teaching of chemical reaction." However, the Examiner interprets a chemical reaction, as recited in Applicants' claims, to "take place when the biologically active agent and the carrier are incubated and the result of the incubation is the formation of a composition that comprises the carrier and the active agent". The Examiner also mentions that Farinas includes a heat step.

Applicants respectfully disagree with this rejection and traverse as follows:

It is well established that a claim is anticipated only if each and every element set forth in the claim is found in the cited reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987); MPEP §2131. Thus, "[t]he identical invention must be shown in as complete detail as contained in the patent claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989); cited by MPEP §2131.

Applicants respectfully contend that the presently claimed methods require that a chemical reaction take place in which covalent bonds are formed or cleaved. In accordance with Applicants' presently claimed invention, the chemical reaction results in the formation of a liquid or solid non-crystalline carrier substance matrix in which a biologically active agent is dissolved or dispersed to a greater degree of saturation than prior to the chemical reaction. Farinas contains no teaching or description of these required elements of Applicants' invention.

The methods that are taught and contemplated by Farinas simply do not constitute or embrace a chemical reaction in which chemical/covalent bonds are formed or broken, as described and claimed by Applicants. Farinas plainly teaches a method in which (1) a drug is

admixed with polymer; (2) a depressed melting temperature is calculated; (3) the drug-polymer admixture is heated to a temperature above the depressed melting temperature that is effective to dissolve the drug in the polymer material; and (4) the admixture is cooled to form the resultant drug reservoir. (Col. 3, lines 40-67 of Farinas).

Unlike Applicants' presently claimed methods, the methods described by Farinas involve the use of a calculated depressed melting temperature, defined by Farinas as "the temperature at which all of the drug [in the drug-polymer admixture] is dissolved in the polymer base." (Col. 6, lines 1-4 of Farinas). Further according to Farinas, "[t]he depressed melting temperature of any particular polymer-drug admixture is thus the temperature at which the drug is completely dissolved in the polymer phase, forming a single phase solution." (Col. 6, lines 6-9 of Farinas).

In Farinas' method, unlike Applicants' presently claimed invention, the drug and polymer in admixture are heated to a temperature that is just higher than the calculated depressed melting temperature, "but not so high as to result in chemical alteration or degradation of any reservoir component." (Col. 6, lines 12-16 of Farinas, emphasis added).

It is submitted that the melting of a component to solubilize or dissolve it in a medium (as described by Farinas) is not a chemical reaction that involves the formation and/or breaking of covalent bonds. Farinas' disclosure that no component in the contemplated method is chemically altered is a direct *teaching away* from Applicants' presently claimed and inventive methods. As such, Farinas does not teach each and every element in Applicants' claimed invention and cannot anticipate the present claims.

The definition of a chemical reaction, as understood by the skilled practitioner in the art, is the breaking and/or formation of chemical/covalent bonds. A chemical reaction generally results in the formation of one or more products that are different from the reactants. Numerous sources of art-recognized definitions of "chemical reaction" indicate that the result of a chemical reaction is a chemical alteration or change of the starting reactants. While the components of Farinas' admixture may undergo a physical change after heating, the teaching of Farinas does not embrace a chemical reaction. Heating an admixture of drug and polymer to

a determined temperature so that the drug is completely dissolved in the polymer material does not constitute a chemical reaction as is appreciated by those having skill in the art as discussed further below.

Illustratively, Applicants provide herewith several sources that define the term “chemical reaction” as would be understood by the ordinarily skilled person in the art. These definitions show that a chemical reaction refers to a change that alters the chemical properties of a substance, as well as to the making or breaking of chemical (e.g., covalent) bonds between atoms or molecules. Tab 1 provides the results from an internet search of the term “chemical reaction” using the universal search engine “Google”. Additional support for the meaning of this term is found in the online encyclopedia, “Wikipedia”. (Tab 2). In addition, the definition of “chemical reaction” as taken from the general chemistry textbook “Chemistry, The Central Science” (1991, Fifth Edition, Eds. T.L. Brown, H.E. LeMay, Jr. and B.E. Bursten, Prentice Hall, Englewood Cliffs, NJ, Glossary, G-4) parallels the several definitions of this term resulting from the internet searches. (Tab 3). In addition, art-recognized definitions of the term “physical change” as compiled by an internet search are provided at Tab 4. As is observed among these definitions, the property of “melting” represents a physical change and not a chemical reaction.

It is respectfully submitted that the foregoing definitions of “chemical reaction” and the recitation of this term in Applicants’ presently claimed methods do not support the Examiner’s interpretation that a chemical reaction automatically takes place when a biologically active agent and a carrier are simply incubated together and a composition is formed. Without a further teaching, such as that of Applicants, that a chemical reaction is performed or initiated on the composition, the composition may be considered a simple solution, admixture, mixture, or dispersion, etc. (depending on the components), in which the components are placed together in physical contact, but are not chemically altered or changed. A physical change may also affect a composition or its milieu; however, this is distinct from a chemical reaction and the two should not be confused. Consequently, Applicants’ presently claimed methods are distinct from that which is taught and described by Farinas and Farinas’ methods.

It is further submitted that a heating step (such as that taught by Farinas) does not constitute a chemical reaction because a chemical change does not occur and/or no new substance is formed as a result of the heating. Rather, according to Farinas, upon heating the drug-polymeric admixture, the drug dissolves in the polymeric material; when the admixture is cooled, the drug, which has not been chemically altered or destroyed by the heating process, is ultimately supersaturated in the drug reservoir. The heating step of Farinas constitutes a physical change in Farinas' described method; however, no chemical reaction is perpetrated on the components of Farinas' disclosed methods. Furthermore, no chemical reaction occurs by merely admixing drug and polymer and by heating as specifically described by Farinas.

In consideration of the above, the method of manufacturing supersaturated transdermal drug delivery systems that is described and contemplated by Farinas does not anticipate Applicants' presently claimed invention. Farinas simply does not disclose or show Applicants' identical invention, considered in its entirety, and in as complete detail as contained in Applicants' present claims. Thus, Farinas does not satisfy the requirements for an anticipating reference under 35 U.S.C. §102.

Because each and every element of Applicants' claims is not found in Farinas, this reference does not anticipate the presently claimed invention. Accordingly, withdrawal of this rejection is respectfully requested.

**The claims satisfy the requirements of 35 U.S.C. §103**

Claims 60, 63, 76, 77, 88, 98, 99, 103, 104 and 106 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 5,906,830 to Farinas et al. (hereinafter "Farinas"). As above, the Examiner has interpreted that a "chemical reaction occurs when the active agent is incubated with a carrier." The Examiner further remarks that "Farinas mixes a carrier and an active agent and the process of mixing necessarily incorporates a wait or incubation period that is not specifically disclosed by Farinas." Based on this, the Examiner opines that it would have been obvious to one of ordinary skill in the art at the time of the invention "to prepare a composition that comprises a carrier and bio-active agent by incubating the carrier and the bio-active agent for some determined time" and that one skilled

in the art would be motivated to do so with “the expectation of producing a bioactive composition comprising a drug and carrier.”

Applicants respectfully disagree that Farinas makes obvious the presently claimed invention and traverse the rejection.

In the Remarks above, Applicants have set forth a detailed discussion directed to the fact that, in accordance with the presently claimed invention, a chemical reaction does not occur by incubating an active agent with a carrier and waiting for a determined period of time for a composition to form. Farinas does not teach, suggest, or contemplate a chemical reaction in the methods disclosed and described in the cited patent. Rather, Farinas teaches a physical, and not a chemical, change in which a drug is solubilized in a polymeric material after raising the temperature of the admixture of the drug and polymeric material to a temperature just higher than the calculated depressed melting temperature. As discussed herein above, Farinas specifically *teaches away* from the notion of a chemical reaction in the sense of forming and/or breaking chemical/covalent bonds as required by Applicants. This is clearly stated in Farinas at Col. 6, lines 12-16, as follows:

An admixture of polymer and drug is then heated to a temperature just higher than the calculated depressed melting temperature, but not so high as to result in chemical alteration or degradation of any reservoir component. (Emphasis added).

In view of a consideration of the complete teachings of Farinas, it is clear that the admixed components of Farinas' method do not undergo a chemical reaction as this term is known and understood by those having skill in the art.

Regarding the Examiner's statement that Applicants' claims do not say how the chemical reactions or “processes came to be, or the agents that aid in the reaction to bring about the process”, it is respectfully submitted that the rejected claims depend from and further limit the currently presented base claims and, as such, contain all of the limitations that are set forth in these base claims, which are novel and patentably distinct from Farinas. It is submitted that the currently presented claims fully describe Applicants' inventive methods of preparing a



biologically active composition involving the formation of a non-crystalline carrier matrix comprising biologically active composition saturated as recited in the matrix, as supported by the disclosure of the instant specification. Indeed, Farinas neither teaches nor suggests Applicants' methods in which a non-crystalline carrier matrix is formed as a result of chemical reaction and in which a biologically active agent is present in the matrix up to a second degree of saturation that differs from the degree of saturation prior to the chemical reaction.

For rejection under 35 U.S.C. §103, a cited reference must be considered in its entirety, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1552 (Fed. Cir. 1983); MPEP §2141.03. Thus, the Office cannot pick and choose among isolated aspects of the reference, but must consider each reference as a whole. *In re Fitch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992); *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988). A consideration of Farinas for all that it teaches shows that Farinas does not make obvious Applicants' presently claimed invention.

In addition, for analysis under 35 U.S.C. §103, it is essential to consider all of the elements of the claimed invention. It is impermissible to compare the cited references with what the viewer interprets as the "gist" of the invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1548 (Fed. Cir. 1983); *Jones v. Hardy*, 727 F.2d 1524, 1530 (Fed. Cir. 1984); and MPEP §2141.02. Each express claim limitation must be taken into account. *See, e.g., Bausch & Lomb v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 447-49 (Fed. Cir. 1986); MPEP §2141.02. All claim limitations must be taught or suggested by the cited art reference. M.P.E.P. 143.03.

Here, the currently presented claims, as supported by the disclosure of the instant specification, clearly describe methods comprising a chemical reaction or process that results in the formation of a liquid or solid non-crystalline matrix comprised of biologically active agent and carrier substance(s), wherein the degree of saturation of the biologically active agent is changed as a result of the chemical reaction relative to the degree of saturation of the active agent prior to the chemical reaction. In contrast, Farinas describes a method in which a specific temperature elevation allows a drug component of an admixture to dissolve in polymer material such that the drug is *physically changed* to a soluble state. Farinas' method takes

place in the absence of chemical alteration or degradation of the components of the method. Accordingly, Farinas' method does not involve a chemical reaction as described by Applicants and as understood by those having skill in the art.

With further regard to the processes recited in claims 60 and 88, Applicants have shown supportive teaching and disclosure in Applicants' specification in the above Remarks related to the §112 rejection. As discussed above, all of the currently presented claims are fully supported by the specification along with and in consideration of standard practice and routine knowledge of the skilled artisan at the time of the present invention. All of the currently presented claims, considered as a whole, are patentably distinguished over the teachings and disclosure of Farinas.

In view of the clear distinctions between Applicants' presently claimed invention and the teachings and disclosure of Farinas, Applicants respectfully assert that Farinas does not negate the patentability of the presently claimed invention. It is therefore respectfully requested that the § 103(a) rejection be withdrawn.

The Examiner has responded to Applicants' previously filed arguments. (05/10/05 Office Action, pp. 6-7). It is respectfully submitted that the Examiner has mischaracterized a chemical reaction in the instant application as involving "the incubation of a biologically active agent with a carrier or with two or more carriers." In this respect, the Examiner has further indicated that Farinas discloses a chemical reaction.

Applicants have explained in detail above, and provided as enclosures herewith, the definition of the term "chemical reaction" as known and understood by the skilled practitioner in the pertinent art. Applicants' presently claimed invention involves more than merely "incubating a biologically active agent with carrier". To reduce Applicants' presently claimed methods to the foregoing is to improperly disregard the need to consider as a whole all of the recited elements of Applicants' claims. Applicants' claims recite a chemical reaction as described by Applicants and as understood by those having skill in the art. "Incubating a biologically active agent with a carrier", without anything more, does not constitute a chemical reaction and does not reflect all of the recited elements of Applicants' presently claimed

invention considered in its entirety. The entirety of Applicants' claimed method, including all of the recited elements therein, must be considered in making a determination of patentability in accordance with MPEP §2141.02.

Applicants' invention involves methods in which a biologically active agent, present up to a first degree of saturation, carrier substance(s), or a composition thereof, is/are subjected to a chemical reaction involving the formation or cleaving of covalent bonds to produce a new product, i.e., a liquid or solid non-crystalline carrier matrix in which the biologically active agent is present up to a second degree of saturation that is greater than the first and from which the biologically active agent does not precipitate. Applicants' invention requires that a chemical reaction be performed or initiated to form a non-crystalline carrier matrix as a new, more complex product resulting from the chemical reaction. Farinas does not suggest or teach a chemical reaction to form a carrier matrix as described by Applicants and does not remotely teach or disclose Applicants' invention as presently claimed.

The Examiner also notes on page 7 of the Office Action that the formation of a covalent bond is not the same as breaking a covalent bond. While Applicants do not disagree with this statement, it is not particularly pertinent to the presently claimed invention in which the chemical reaction that takes place may involve the formation and/or cleavage of covalent bonds in order to form the described non-crystalline carrier matrix with active agent. Processes that can constitute a chemical reaction in accordance with Applicants' presently claimed invention are disclosed by Applicants and are understood by the skilled practitioner. Moreover, the conditions used to achieve such chemical reactions are in accordance with standard reference literature. It is thus respectfully submitted that Applicants have provided ample description and exemplification throughout the instant specification to support the recitation of chemical reaction in the presently claimed invention.

Finally, Applicants take note of the additional art made of record and not relied on, as well as the Examiner's implicit recognition of the patentable distinctions between Applicants' claimed invention and this cited art.

Applicants: Ake R. Lindahl, *et al.*  
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### CONCLUSION

Applicants respectfully submit that the application is now in condition for allowance. An action progressing this application to issue is courteously urged.

Should any additional fees be deemed to be properly assessable in this application for the timely consideration of this amendment and response, or during the pendency of this application, the Commissioner is hereby authorized to charge any such additional fee(s), or to credit any overpayment, to Deposit Account No. **50-0311**, Reference no. **28069-558 NATL**, Customer Number: **35437**.

Should an extension of time further to that requested be required for the timely consideration of this Amendment and response, the Commissioner is hereby authorized to grant any such extension of time as may be necessary, and to charge any additional fee(s) owed by Applicants for such extension of time, to the above-mentioned Deposit Account, Reference and Customer Numbers.

If the Examiner believes that it would be helpful to discuss the application to advance the prosecution of the application and claims to allowance, the Examiner is respectfully requested to telephone applicants' undersigned representative at (212) 692-6742 and is assured of full cooperation in this effort.

Respectfully submitted,

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